## REMARKS

Claim 6 has been cancelled, without prejudice.

Claim 1 has been amended to recite that the recombinant organism is "carotenoid producing." Support for this amendment is found in the specification at, for example, pp. 3-4, ¶ [0008].

Claim 1 has further been amended to recite that the active oxygen species-quenching factor is encoded by a polynucleotide that is SEQ ID NOs: 1-4, or 8 or that hybridizes under high stringency conditions to the complement of SEQ ID NOs: 1-4, or 8, wherein the hybridizing polynucleotide encodes a polypeptide having mitochondrial SOD, cytoplasmic SOD or catalase activity. Support for this amendment is found in original claims 1, 6 and 7, and in the specification at, for example, pp. 4-5, ¶¶ [0011]-[0012]. *See*, *In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§608.01(o) and (l).

Claim 1 has also been amended for the purposes of clarity to replace the phrase "a gene for one or more" with the phrase "at least one polynucleotide encoding." Support for this amendment is found in the specification at, for example, pg. 14, ¶ [0040].

Claim 7 has been amended to remove the recitation of a Markush group and to recite only --SEQ ID NO: 1--. Support for this amendment is found in the specification at, for example, pp. 7-8, ¶ [0021].

Claims 38-43 have been added. Support for these claims is found in original claims 1, 6 and 7, and in the specification at, for example, pp. 4-5, ¶¶ [0011]-[0012]. *Id.*

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

**Objections to the Claims**

Claims 6 and 7 were objected to under 37 CFR §1.75(d) (1) "as being in improper form because the claim states an improper Markush [group]." (Office Action at 2). In making the objection, the Examiner asserted that:

> Superoxide dismutase and catalase are independent functional [activities]. Thus, the member[s] of the Markush Group of claim 6 do not share a common structural feature, and function. Similarly, the polynucleotide sequences of SEQ ID NO's: 1-4, 6 and 8 (claim 7) are independent chemical compounds and do not share a common structure feature for the stated utility. *Id.*

Claim 6 has been cancelled, without prejudice. Accordingly, the objection with regards to claim 6 has been rendered moot and should be withdrawn.

Claim 7 has been amended to recite only SEQ ID NO: 1, and no longer recites a Markush group. Accordingly, the objection to claim 7 has been rendered moot and should be withdrawn.

Claims 6 and 7 were also objected to "because they contain non-elected subject matter." (Office Action at 2).

Claim 6 has been cancelled, without prejudice. Accordingly, the objection with regards to claim 6 has been rendered moot and should be withdrawn.

As noted above, claim 7 has been amended to recite only SEQ ID NO: 1. Accordingly, the objection has been rendered moot and should be withdrawn.

**§ 101 Rejection**

Claims 1-3, 6, and 7 were rejected under 35 USC §101. (Office Action at 3). In making the rejection, the Examiner asserted that "[c]ultivating a recombinant organism containing [a] disabling mutation to one or more gene[s] encoding [an] 'active oxygen species-quenching factor' would not be expected to produce carotenoids, and thus, the claimed method is inoperative." (*Id.*). The Examiner suggested that "[a]mending the claim to indicate that the organism is carotenoids producing [sic] would obviate this rejection." (*Id.*).

With a view towards furthering prosecution and in accordance with the Examiner's recommendation, claim 1 has been amended to specify that the recited organism is a "carotenoid producing" organism. Accordingly, it is respectfully submitted that the rejection is rendered moot and should be withdrawn.

**§112, Second Paragraph Rejection**

Claims 1-7 were rejected under 35 USC §112, second paragraph. (Office Action at 5). In making the rejection, the Examiner asserted that "[t]he phrase 'active oxygen species-quenching factor' in claim 1 renders the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired." (*Id.*).

To reject a claim under the second paragraph of 35 USC §112, it is incumbent on the examiner to establish that one of ordinary skill in the pertinent art, when reading the claims in light of the supporting specification, would not have been able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims. *Ex parte Wu*, 10 USPQ2d 2031, 2033 (BPAI 1989). This, the Examiner has not done. The Examiner has merely made an assertion with out any factual support of any kind. For this reason alone, it is respectfully submitted that the rejection should be withdrawn.

Further, the specification discloses that "active oxygen species-quenching factors" are well known in the art and include SOD and catalase. *See* pp. 2-3, ¶ [0004]. Further, we note that the specification clearly discloses that "[t]he active oxygen species-quenching factor(s) is(are) mitochondrial superoxide dismutase (SOD), cytoplasmic superoxide dismutase (SOD), and/or catalase." Thus, it is respectfully submitted that one of ordinary skill in the art would readily ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims, particularly with regards to the term "active oxygen species-quenching factor." For this reason also, the rejection should be withdrawn.

In making the rejection, the Examiner further asserted that "[c]laims 1-3, 6, and 7 are incomplete for omitting essential elements.... The omitted elements are: recombinant carotenoids producing organism." (*Id.*).

With a view towards furthering prosecution, claim 1 has been amended to recite that the recombinant organism is "carotenoid producing." Accordingly, the rejection is rendered moot and should be withdrawn.

**§112, First Paragraph, Written Description Rejection**

Claims 1-6 were rejected under 35 USC §112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (Office Action at 3). In making the rejection, the Examiner contended that "[t]here is no disclosure of any particular structure to function/activity relationship among the three disclosed species." (*Id.* at 3-4).

Initially, we note that claim 6 has been cancelled, without prejudice, accordingly, the rejection with regards to claim 6 is rendered moot and should be withdrawn.

With a view towards furthering prosecution, claim 1 has been amended to recite specific polynucleotide sequences as well as the specific activities of the polypeptides encoded by the polynucleotide sequences (mitochondrial SOD, cytoplasmic SOD and catalase activities). It is respectfully submitted that claim 1, as amended, is clearly tied to a structure (*i.e.*, SEQ ID NOs: 1, 2, 3, 4, 6, and 8) and that this structure correlates with the recited activities. Accordingly, the rejection is rendered moot and should be withdrawn.

**§112, First Paragraph, Enablement Rejection**

Claims 1-7 were rejected under 35 USC §112, first paragraph. (Office Action at 4). In making the rejection, the Examiner asserted that "the claims are broader than the enablement provided by the disclosure with regard to a method of producing carotenoids using any recombinant organism in which *any gene* encoding superoxide dismutase activity, catalase, or any other 'active oxygen species-quenching factor' [is disrupted]." *Id.* (emphasis added).

The Examiner acknowledged, however, that the specification is enabling for "a method for producing carotenoids by culturing *P. rhodozyma* in which the gene(s) encoding mitochondrial and/or cytoplasmic super oxide dismutase and/or catalase [have] been disabled." *Id.* The Examiner further acknowledged that "[t]he specification provides guidance and examples in the form of an assay to clone the mitochondrial and cytoplasmic superoxide mutase [sic] as well as partially clone a catalase from *P. rhodozyma*, a carotenoid producing organism, and construct a disabling cossets [sic] to produce the recombinant *P. rhodozyma* with disabled gene(s) and the use of the genetically modified *P. rhodozyma* in the production of carotenoids." *Id.*

Initially, we note that claim 6 has been cancelled, without prejudice. Accordingly, the rejection with regards to claim 6 is rendered moot and should be withdrawn.

With a view towards furthering prosecution, claim 1 has been amended to recite an organism having a polynucleotide encoding an active oxygen species-quenching factor that is disrupted, wherein the factor is encoded by specific

polynucleotide sequences or polynucleotide sequences that hybridize to the complement of the specifically defined sequences under high stringency hybridization conditions (wherein the hybridizing polynucleotide encodes a polypeptide having cytoplasmic SOD, mitochondrial SOD or catalase activity). Accordingly, claims 1-7 recite specific sequences that correspond to the disrupted polynucleotides and that can be used in constructing disruption cassettes. As the Examiner acknowledged, "molecular biological techniques and genetic manipulation [techniques] to disable specific gene(s) in an organism ***are known*** in the prior art and the skill of the artisan are well developed." *Id.* Further, it is undisputed that the specification discloses the polynucleotide sequences for SEQ ID NOs: 1, 2, 3, 4, 6, and 8, as well as Examples and assays for cloning these polynucleotides and detailed conditions for carrying out hybridization under stringent conditions. *See* Sequence Listing, Examples 1-14 and pp. 4-5, ¶¶ [0011]-[0012].

In view of the Examiner's own recognition that the specification provides "guidance and examples" for cloning the recited polynucleotides, constructing the recited disruption cassettes for disabling the recited polynucleotides, using the recombinant organism in the production of carotenoids, and that the techniques used are "known in the prior art" and "the skill of the artisan are well developed," it respectfully is submitted that claims 1-7 are fully enabled. Accordingly, for this reason, withdrawal of the rejection is respectfully requested.

**Obvious-Type Double Patenting Rejection**

Claims 1-6 were rejected under the judicially created doctrine of obviousness-type double patenting. (Office Action at 3). In making the rejection, the Examiner alleged that claims 1-6 are "unpatentable over claims 1-12 of U.S. Patent No. 6,696,293" (*Id.*). The Examiner further asserted that "[i]t would have been obvious to one of ordinary skill in the art to utilize the claimed cell according to claims 7-12 which is made according to the method of claims 1-6 in a method to make [carotenoids] (claims 1-6)." *Id.*

Initially, we note that claim 6 has been cancelled, without prejudice. Accordingly, the rejection with regards to claim 6 is rendered moot and should be withdrawn.

As is well settled, an obvious-type double patenting rejection compares the ***claims*** in the rejected application with the ***claims*** in an issued or to be issued patent. Also, we note that the analysis used for an obvious-type double patenting rejection parallels that used for a rejection under 35 USC §103. *See*, MPEP §804 (II)(B)(1). Further, "to establish *prima facie* obviousness of a claimed invention, ***all claim limitations*** must be taught or suggested by the prior art." MPEP §2143.03 citing *In re Royka*, 180 USPQ 580 (CCPA 1974). There must be some suggestion which would have "impelled" one to do what the applicants have done. *Ex parte Levengood*, 28 USPQ2d 1300, 1301-02 (BPAI 1993). Thus, the rejection should include reasons why a person of ordinary skill in the art would conclude that the invention defined in the claim in issue is an obvious variation of the invention defined in a claim in the patent.

With a view towards furthering prosecution, claim 1 has been amended to recited that the active oxygen species-quenching factor is encoded by specific polynucleotide sequences (SEQ ID NOs:1, 2, 3, 4, 6 and 8) and those that hybridize to these sequences (and that encode polypeptides that have SOD or catalase activity). Claims 1-12 of U.S. Patent No. 6,696,293 ("the '293 patent") recite a microorganism having a reduced level of alternative oxidase (AOX) expression. One of skill in the art will readily recognize that AOX is a distinctly different enzyme compared to the polypeptides encoded by the presently claimed polynucleotide sequences (*e.g.*, SOD or catalase). For example, SOD and catalase each catalyze different reactions than AOX and are encoded by distinct polynucleotide sequences (compare SEQ ID NOs: 1-4, 6 and 8 with SEQ ID NO: 2 of the '293 patent).[1/] Accordingly, it is respectfully submitted that one of skill in the art would not have been "impelled" to substitute the microorganism having reduced AOX expression for the recombinant organism having the genes encoding for polypeptides having mitochondrial SOD, cytoplasmic SOD and/or catalase activity disrupted with a disruption cassette, for use in the process of instant claims 1-5, as amended. For this reason, we respectfully submit that the rejection is rendered moot and should be withdrawn.

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1/ We note, for example, that AOX "plays a substantial role in transferring an electron from the ubiquinone pool to an $H_2O$ molecule by using an oxygen molecule as an acceptor." '293 patent at Col. 2, lns. 7-10. SOD, on the other hand, catalyzes "the disproportioning of $O_2$•, producing $O_2$ and $H_2O_2$." pg. 11, ¶ [0032].

For the reasons set forth above, entry of the amendments, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned attorney.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box. 1450 Alexandria, VA 22313-1450, on July 19, 2004.

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Respectfully submitted,

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